

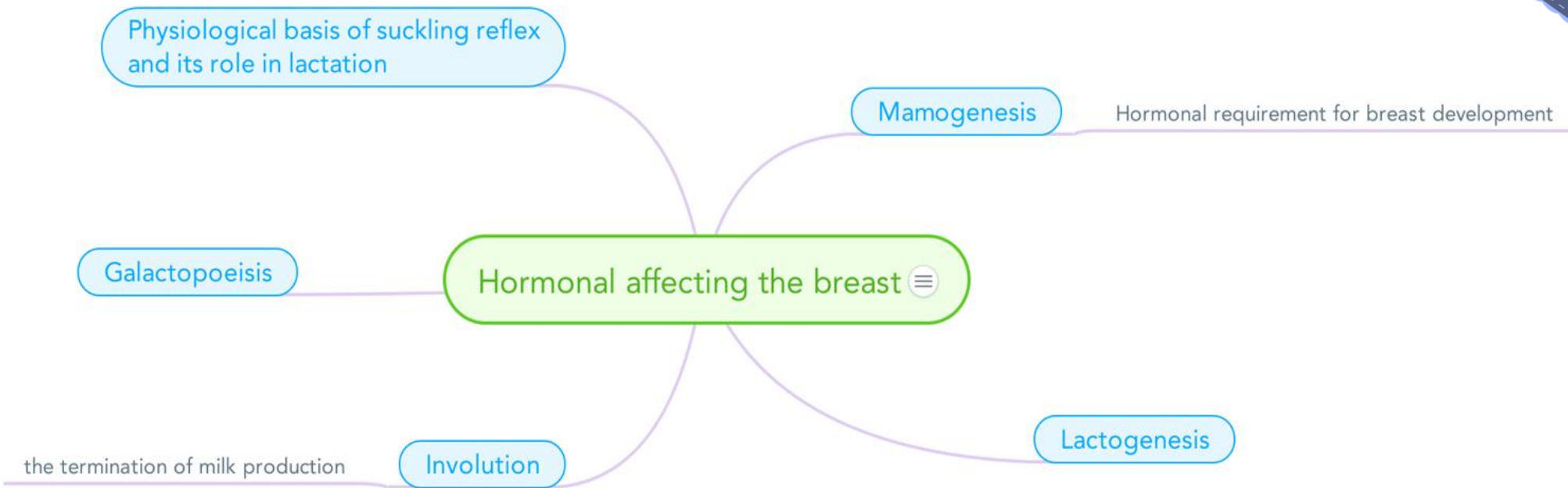


# Hormonal Affecting the Breast

## Reproductive Block

Please check out this link before viewing the file to know if there are any additions/changes or corrections [Physiology Edit File](#)

- Important
- Further explanation



Dr. Al Otaibi recommend us to study also this handout (5 pages) which is cover all hormones that affect the breast: [Click here](#) to download.

# Role of Hormones in Breast

Endocrine system plays a major role in synchronizing development (mamogenesis) and function (lactogenesis) of mammary gland with reproduction. Three categories of hormones:

## 1-Reproductive hormones (endocrine)

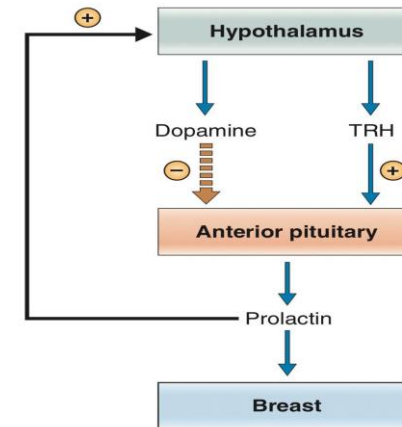
Estrogen, progesterone, prolactin, oxytocin and hpl

## 2-Metabolic hormones (endocrine)

GH, corticosteroids, thyroxin, PTH and insulin

## 3-Mammary hormones (autocrine)

GH, prolactin, parathyroid hormone-related protein (PTHrP) and leptin



**Table 9-5** Factors Affecting Prolactin Secretion

Stimulatory Factors	Inhibitory Factors
Pregnancy (estrogen)	Dopamine
Breast-feeding	Bromocriptine (dopamine agonist)
Sleep	Somatostatin
Stress	Prolactin (negative feedback)
TRH	
Dopamine antagonists	



## Endocrine Control of Lactation:

### ● Milk Production Reflex:




**Prolactin** is a key lactogenic hormone, stimulates initial alveolar milk production, inhibits epithelial cell loss and maintain cellular differentiation

### ● Milk Ejection Reflex:

**Oxytocin** contracts the myoepithelial cells, forcing milk from the alveoli into the ducts and sinuses where it is removed by the infant

# Hormonal Stimulating Breast

## Mammogenesis and lactogenesis

During puberty	During pregnancy	During lactation
<p>(Mammogenesis)</p> <p>Ovarian hormones stimulate mammary growth</p> <ol style="list-style-type: none"> <li>1-Estrogen stimulate proliferation of ducts and deposition of fat</li> <li>2-Progesterone stimulate development of lobules</li> <li>3- Prolactin also has role</li> </ol> 	<p>( Mammogenesis)</p> <ol style="list-style-type: none"> <li>1- HCG from placenta keep the corpus luteum secrete estrogen and progesterone</li> <li>2-Prolactin with estrogen and progesterone stimulate growth and development of mammary alveoli and also HPL has a role</li> </ol> <p>Result from these two actions is the <b>complete development of glandular tissue.</b></p> 	<p>(Lactogenesis)</p> <p>Although prolactin levels are high during pregnancy, lactation does not occur due estrogen and progesterone <b>down-regulate prolactin receptors in breast</b> and <b>block the action of prolactin.</b> At parturition progesterone and estrogen levels drop and inhibitory action cease. Prolactin stimulate lactogenesis and lactation occur.</p> 

### Stages of Development of The Mammary Gland



\***Involution:** This is when the breasts stop producing milk completely after weaning.

# Mamogenesis (Breast Development)



## Reproductive Hormones (Direct effect)

### Estrogen (placenta)

- 1-Growth & branching of ductal system (with GH)
- 2- Fat deposition in the stroma

### Progesterone (placenta)

- Growth of lobule-alveolar system  
(budding of alveoli and secretory changes in epithelial cells)

### Lobule-Alveolar System

The function of the cells of the alveoli is to remove nutrients from the blood and transform these nutrients into the components of milk.

### Prolactin (anterior pituitary)

- 1-Its level increases during pregnancy from fifth week until birth (10-20 times)
- 2- Its main function is milk production
- 3-Sudden drop in Estrogen & Progesterone after delivery allows milk production

controlled mainly by hypothalamic hormone ( PIH or dopamine + TRH)

- It stimulates mammary gland growth, proliferation of alveolar epithelial cells, and gene expression which induce the synthesis of milk components (casein, lactose and lipids)

### Human placental lactogen (human chorionic somatomammotropin "Hcs")

- 1-Facilitate mammogenesis
  - 2- Delay milk production
- \*It supports the prolactin during pregnancy (lactogenic properties)
  - \*It Suppresses the prolactin by stimulating the dopamine.



# Lactogenesis

**Definition:** cellular changes by which mammary epithelial cells are converted from a non secretory state to a secretory state.

## Stages of Lactogenesis

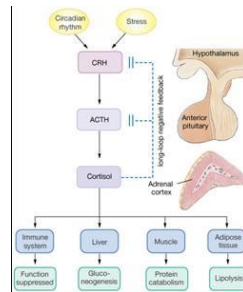
### Lactogenesis 1

Cytologic and enzymatic differentiation of alveolar epithelial cells.

Starts in mid pregnancy and characterized by expression of many genes involved in synthesis of milk components (increase in the uptake transport systems for amino acids, glucose, and calcium required for milk synthesis).

Hormones involved:

1. **Progesterone** (suppresses milk secretion)
2. **Prolactin** and/ or placental lactogen
3. **Growth hormone**
4. **Glucocorticoids (Cortisol)**



### Lactogenesis 2

Copious secretion of all milk components starts 2-3 days postpartum

Around parturition withdrawal of **progesterone** + high level of **prolactin** leads to:

- 1-Further increase in expression of milk protein genes
- 2- Glands absorb increased quantities of metabolic substrates from the blood.
- 3-Movement of cytoplasmic lipid droplets and casein into alveolar Lumina
- 4-Transfer of immunoglobulin
- 5- Secretion of colostrum followed by milk

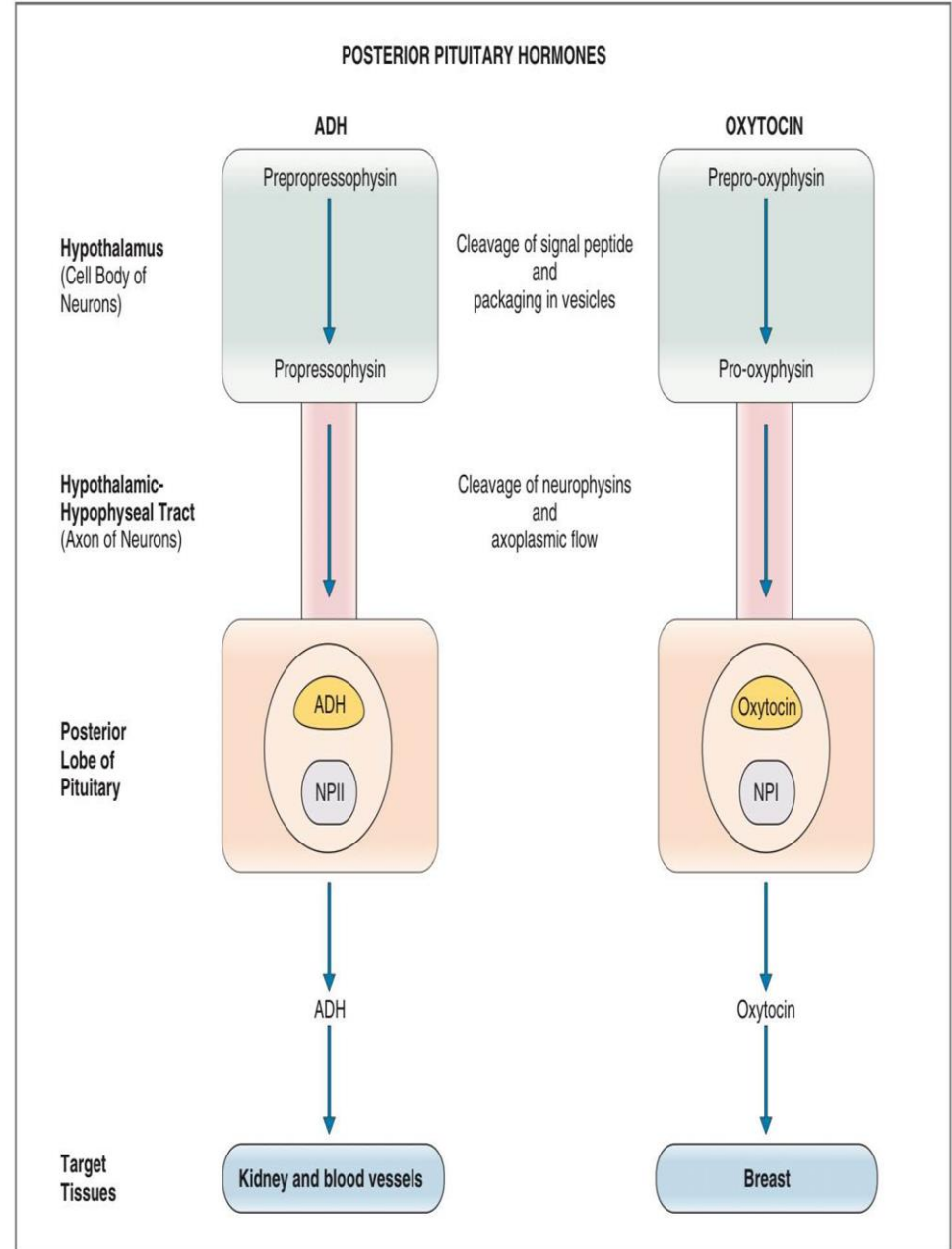
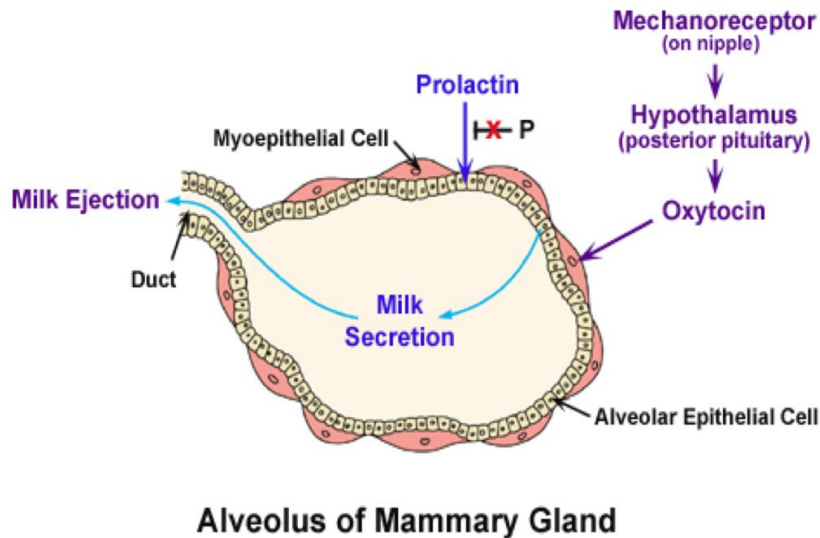
Suckling stimulates further increase in expression of genes involved in milk secretion with expansion of alveolar epithelium  
Lactation is maintained by removal of milk

**2 hormones involved**

- Prolactin** (milk production)
- Oxytocin** (milk let-down)

**Table 9-7** Factors Affecting Oxytocin Secretion

Stimulatory Factors	Inhibitory Factors
Suckling Sight, sound, or smell of the infant Dilation of the cervix Orgasm	Opioids (endorphins)





# Hormonal Regulation of Lactogenesis

## Types of hormones

### Metabolic hormones ( direct effect )

#### **GH**

- 1-Can be produced locally
- 2-its secretion is stimulated by progesterone
- 3-Increases production of IGF-1 by the liver and locally.
- 4-Mediate cell survival and ductal growth

#### **Corticosteroids**

- 1-Increases during pregnancy (five fold)
- 2-Involved in breast development (permissive action on milk protein synthesis), induce differentiation of the organelles of the secretory epithelial cell.

#### **Thyroxin**

- 1-Essential for milk production
- 2-Thyroxin & TSH level decreases during lactation
- 3-TRH increases leading to stimulation of PRL (nasal administration to treat inadequate lactation )

#### **insulin**

- 1-Low during lactation
- 2-Shunt of nutrients from storage depots to milk synthesis

### Mammary hormones

#### **GH**

Progesterone stimulates its secretion, helps in growth of mammary glands

#### **Leptin**

- 1-Increases during pregnancy (increase adipose tissue)
- 2- Decreases with lactation

#### **PTHrP**

- 1-Increases during lactation
- 2-Mobilizes bone calcium
- 3-Increase in alkaline phosphatase

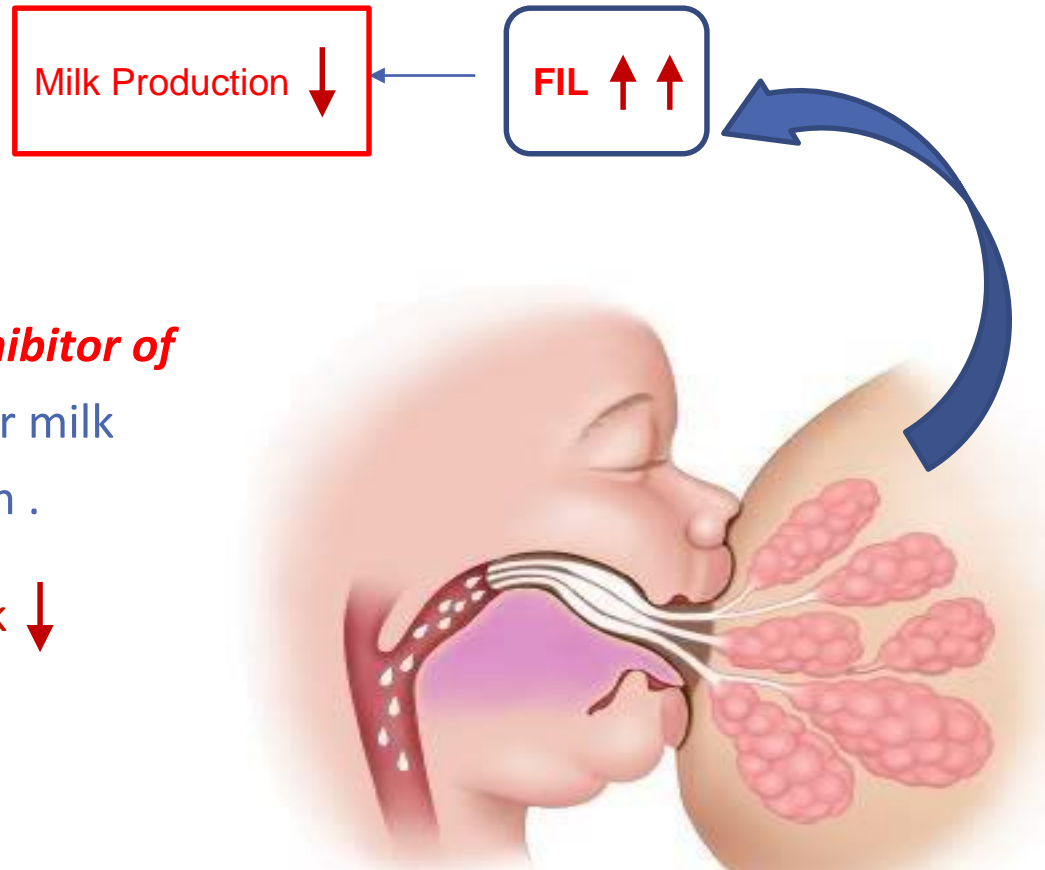




# Autocrine Control of Lactation



- A protein factor called **feedback inhibitor of lactation (FIL)** is secreted with other milk components into the alveolar lumen .
- **FIL**, insensitive to prolactin → milk ↓ production



# Galactopoiesis



**Definition :** Maintenance of lactation once lactation has been established starts 9-15 days postpartum

## Hormonal Regulation of Galactopoiesis

**Prolactin:** milking-induced surge is a direct link between the act of nursing (or milk removal) and the galactopoietic hormones involved in maintaining lactation.

**Growth Hormone:** support increase in synthesis of lactose, protein, and fat in the mammary gland

**Glucocorticoids:** galactopoietic in physiological doses

**Thyroid Hormones:** galactopoietic

**Estrogen** in very low doses is galactopoietic

**Progesterone** alone has no effect on galactopoiesis because there are no progesterone receptors in the mammary gland during lactation



### Galactopoietic Hormones:

- -parathyroid hormones
- -Insulin

### Milk production

- Milk production is "use it or lose it" process.
- The more often and effectively the baby nurses, the more milk will be produced
- Milk production <100 ml/day in day 1 postpartum
- Milk production by day 3 reaches 500 ml/day
- Milk composition changes dramatically ( $\downarrow$ Na<sup>+2</sup>& Cl<sup>-</sup>) due to closure of tight junctions that block paracellular pathway

### AAP RECOMMENDATION

Exclusive breastfeeding for the first six months of life

Continued breastfeeding for at least one year, 'As long as is desired by mother and child'.



# Suckling Reflex

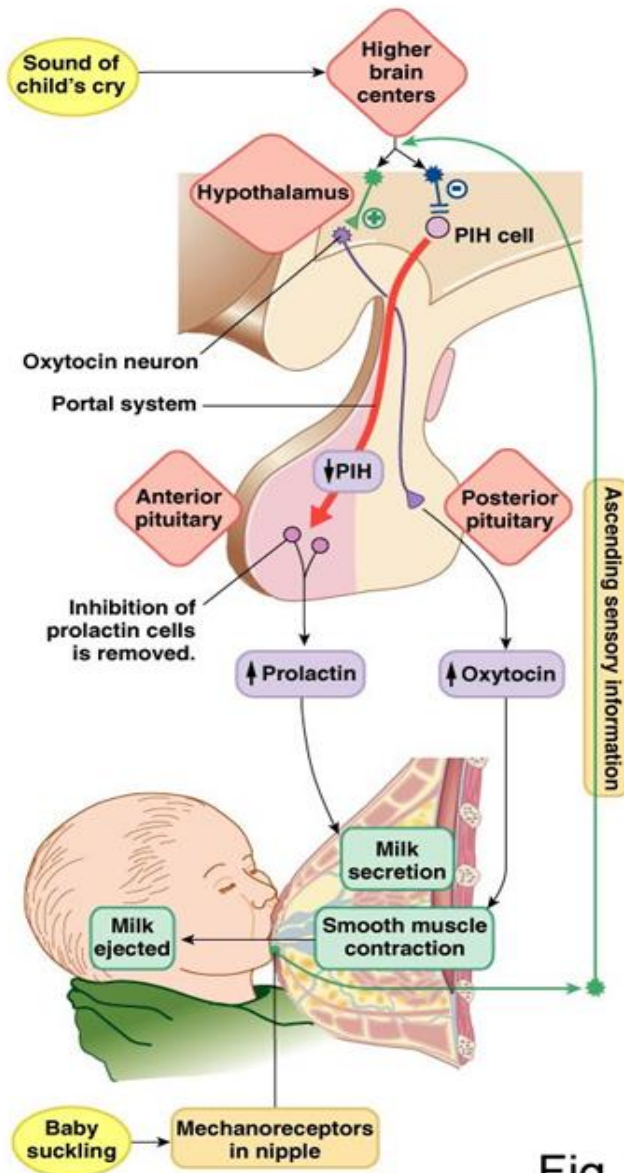


Fig. 2

Stimulus from sucking pass from breast to spinal cord and then to hypothalamus

Neurons from spinal cord inhibit the dopamine release from arcuate nucleus → prolactin will increase and lead to milk production in breast

Neurons from spinal cord will inhibit the arcuate nucleus and preoptic area in hypothalamus → this will decrease GnRH → decreased the stimulation of ovary → inhibit the ovarian cycle

Neurons from spinal cord produce stimulate production and release of oxytocin from supraoptic nucleus and paraventricular nuclei that through the blood into myoepithelial cells and breast

\*Estrogens and Progesterone Throughout pregnancy, estrogens and progesterone stimulate the growth and development of the breasts, preparing them for lactation.

\*prolactin levels steadily increase from the 5th week of pregnancy until the birth of the baby

\*The basal level of prolactin secretion returns to the nonpregnant level during the next few weeks after parturition

\* Final development of the breasts into milk-secreting organs also requires progesterone.

\*The fluid secreted during the first few days after parturition is called colostrum

\*Prolactin stimulates milk production by inducing the synthesis of the components of milk including lactose , casein , and lipids .

\*Prolactin suppresses ovulation and menstruation by inhibiting the hypothalamic GnRH.

\*Lactogenesis 1 : Starts mid pregnancy until parturition and is controlled by prolactin, hPL, progesterone, growth hormone and cortisol.

\*The more often and effectively the baby nurses, the more milk will be produced

\*If milk is not removed, the inhibitor (FIL)collects and stops the cells from secreting any more.

\* - Milk production <100 ml/day in day 1 postpartum

- Milk production by day 3 reaches 500 ml/day

# MCQs

1) Which ONE of the following is released by suckling the nipple?

- A. Cortisol
- B. Dopamine
- C. Oxytocin

2) Which one is the correct?

- A. Progesterone stimulates development of lobules
- B. Estrogen stimulates deposition of fats.
- C. Both

3) Prolactin is controlled mainly by hypothalamic hormone?

- A. PIH
- B. TRH
- C. GHRH

4) All of the following will stimulate milk production except?

- A. Prolactin
- B. Suckling
- C. Progesterone

5) Hormones involved in Mammary Growth?

- A. Catecholamines
- B. Aldosterone
- C. Insulin

**Answers:** 1-C 2-C 3-A 4-C 5-C

Q1 : how does the prolactin cause infertility in both sexes ?

Ans: By inhibition the GnRH

Q2: during pregnancy why there is no lactogenesis ?

Ans: Because estrogen and progesterone down regulate the prolactin receptors in breast and block the action of prolactin

Q3: Mention 3 stimulatory factors of prolactin

Ans: 1- TRH                      2- estrogen                      3- breast feeding

Q4: Mention the role of HPL in mammogenesis ?

Ans: 1- delay milk production (lactogenesis)    2- facilitate mammogenesis

Q5: Mention the possible disease can occur in child due depend on breastfeeding?

Ans: Iron deficiency anemia because mother milk has low amount of iron

Q6: Mention the name of nuclei that release prolactin hormone

Ans: arcuate nuclei

**Done By**

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what are the differences between us ?



**Revised By** Omar AlRahbeeni & Amal Afrah

Thank you for checking our work

**Best Wishes..**